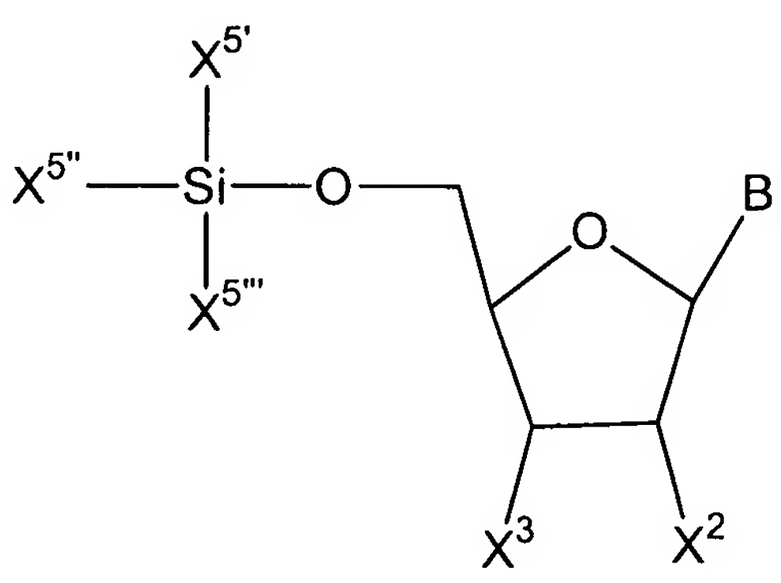
Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

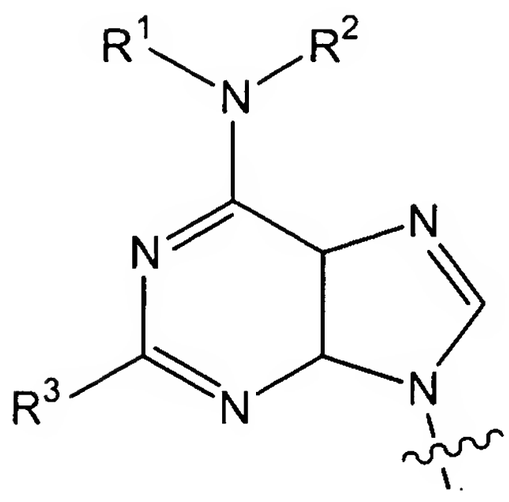
1. (Original) A protected monomer having a formula (I)



(I)

wherein,

B is selected from the group consisting of:



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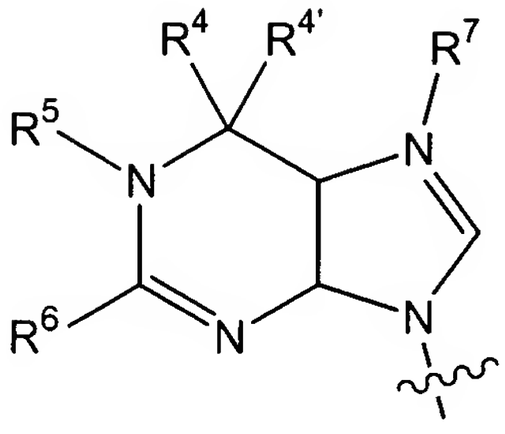

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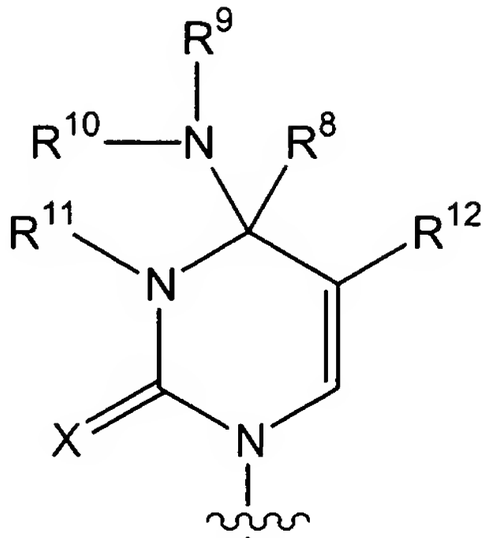

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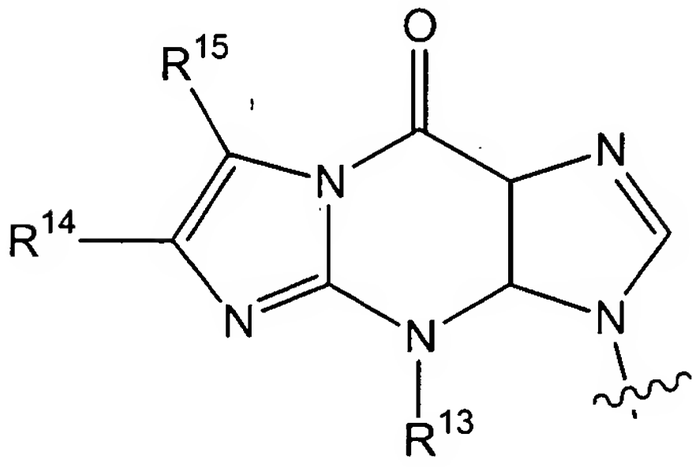

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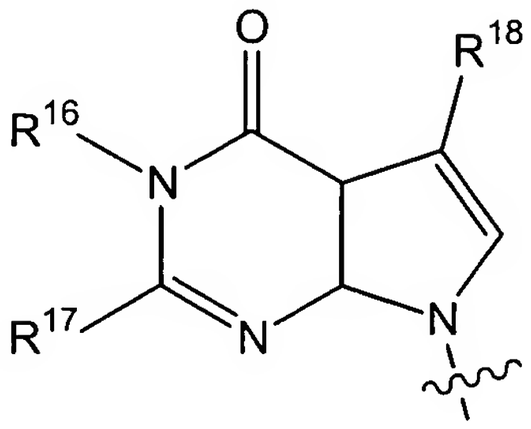

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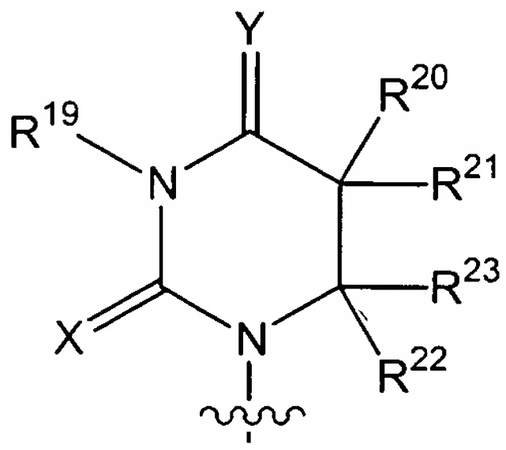

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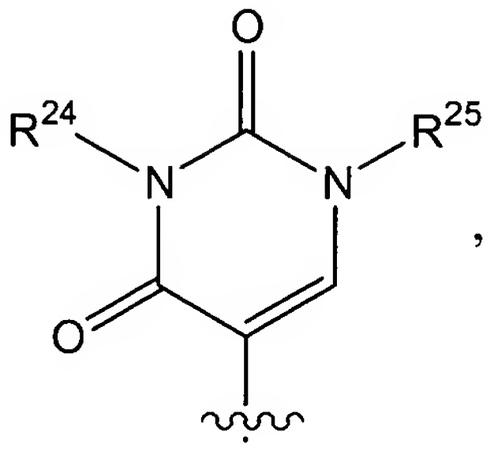

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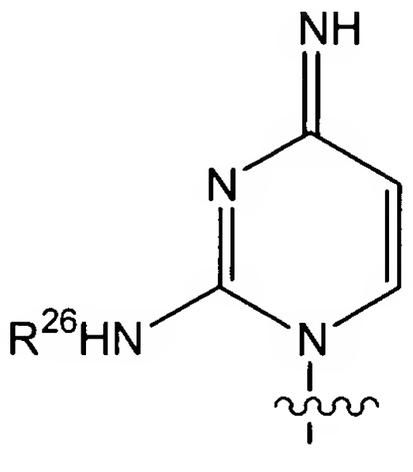
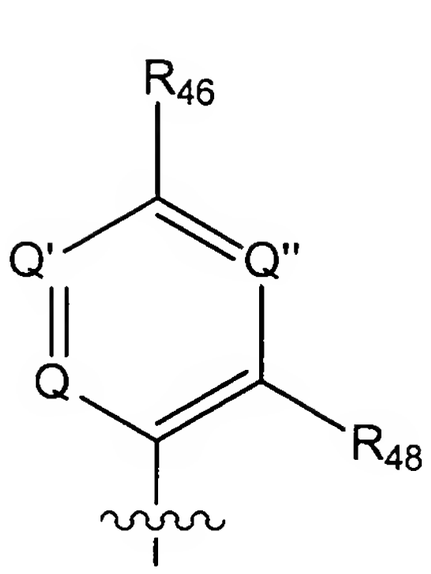


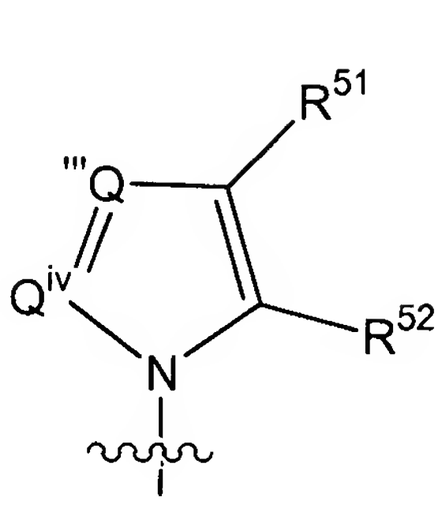
,

anthracenyl, pyrenyl,

R53


R46
Q'
Q''
Q
R48

,


R51
'''Q
Q^iv
N
R52

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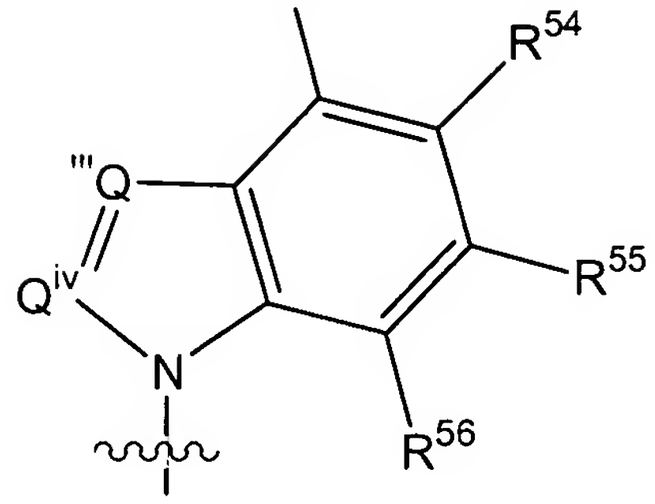
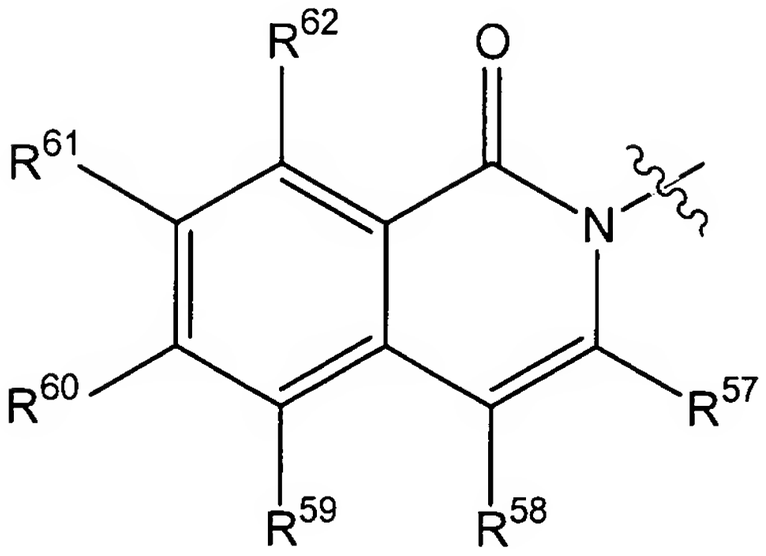
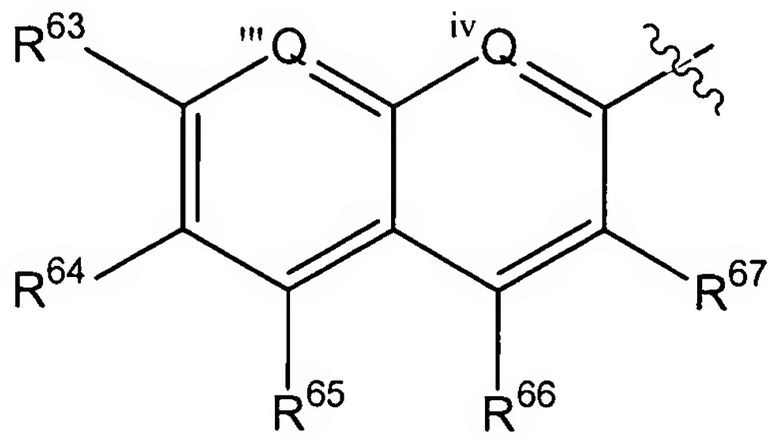
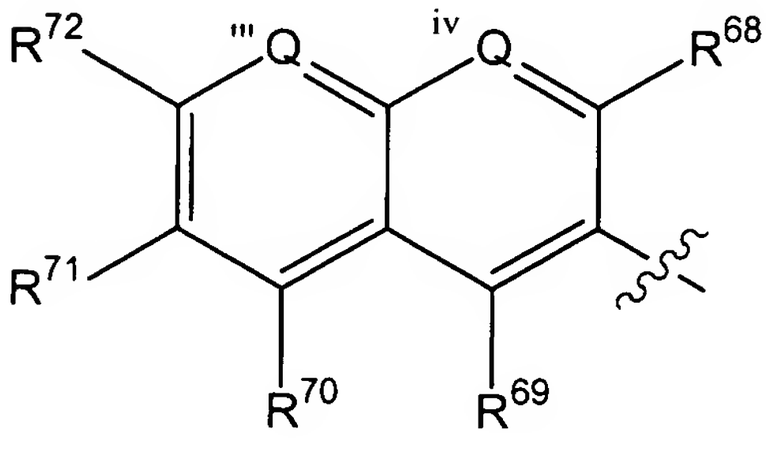

R54
'''Q
Q^iv
N
R55
R56


R62
O
R61
N
R60
R57
R59
R58

,


R63
'''Q
^ivQ
R64
R67
R65
R66

, and


R72
'''Q
^iv
Q
R68
R71
R70
R69

;

X^2 is an ortho ester protecting group, hydrogen, ethers, alkyl ethers, esters, halogens, protected amines, or protected hydroxyl moieties;

X^3 is -O-P(OR^{27})N(R^{28})$_2$ or -O-L-R^{29};

$X^{5'}$, $X^{5''}$, $X^{5'''}$ include at least one alkoxy or siloxy substituent;

R^1 is hydrogen or C_1-C_4 alkyl;

R^2 is hydrogen, C_1-C_4 alkyl, or C_2-C_6 alkenyl optionally substituted with hydroxy, or C(O)NHR^a;

R^3 is hydrogen, halo, C_1-C_4 alkyl, C_1-C_4 thioalkoxy, NH_2, NHR^b, or NR^bR^c;

R^4 when taken together with $R^{4'}$ forms oxo, or R^4 when taken together with R^5 forms a double bond between the carbon and nitrogen atoms to which they are attached;

$R^{4'}$ when taken together with R^4 forms oxo, or is O^-;

R^5 is hydrogen, C_1-C_4 alkyl, or when taken together with R^4 forms a double bond between the carbon and nitrogen atoms to which they are attached;

R^6 is hydrogen, halo, NH_2, NHR^b, or NR^bR^c;

R^7 is an unshared electron pair, or C_1-C_4 alkyl;

R^8 when taken together with R^9 forms a double bond between the carbon and nitrogen atoms to which they are attached, or R^8 when taken together with R^{11} forms a double bond between the carbon and nitrogen atoms to which they are attached;

R^9 is hydrogen, C_1-C_4 alkyl, or when taken together with R^8 forms a double bond between the carbon and nitrogen atoms to which they are attached;

R^{10} is hydrogen or is absent;

R^{11} is hydrogen, C_1-C_4 alkyl, or when taken together with R^8 forms a double bond between the carbon and nitrogen atoms to which they are attached;

R^{12} is hydrogen, formyl, or C_1-C_4 alkyl optionally substituted with hydroxy or protected hydroxy;

R^{13} and R^{14} are each independently hydrogen or C_1-C_4 alkyl;

R^{15} is hydrogen, C_1-C_4 alkyl, or $(CH_2)_nCH(R^d)CH(NHR^e)(COOR^g)$;

R^{16} is hydrogen or C_1-C_4 alkyl;

R^{17} is halo, NH_2, NHR^b, or NR^bR^c;

R^{18} is cyano, $C(=NH)NH_2$, or $CH_2NH(R^h)$;

R^{19} is hydrogen, or C_1-C_4 alkyl;

R^{20} is:

(i) hydrogen;

(ii) hydroxy or protected hydroxy;

(iii) C_1-C_4 alkoxy optionally substituted with $COOR^f$; or

(iv) C_1-C_4 alkyl optionally substituted with hydroxy and/or $COOR^f$, NH_2, NHR^m, or $CONH_2$;

R^{21} is hydrogen, or when taken together with R^{23} forms a double bond between the carbon atoms to which they are attached;

R^{22} is hydrogen;

R^{23} is hydrogen, or when taken together with R^{21} forms a double bond between the carbon atoms to which they are attached;

R^{24} and R^{25} are each, independently, hydrogen or C_1-C_4 alkyl;

R^{26} is $(CH_2)_nCH(R^d)CH(NHR^e)(COOR^g)$;

R^{27} is C_1-C_6 alkyl optionally substituted with cyano, or C_2-C_6 alkenyl;

R^{28} is C_1-C_{10} alkyl;

R^{29} is a liquid or solid phase support reagent;

Q is N or CR^{44};

Q' is N or CR^{45};

Q'' is N or CR^{47};

Q''' is N or CR^{49};

Q^{iv} is N or CR^{50};

R^{44} is hydrogen, halo, hydroxy, nitro, protected hydroxy, NH_2, NHR^b, or NR^bR^c, C_1-C_6 alkyl, C_6-C_{10} aryl, C_6-C_{10} heteroaryl, C_3-C_8 heterocyclyl, a ligand, a tethered ligand, or when taken together with R^{45} forms $-OCH_2O-$;

R^{45} is hydrogen, halo, hydroxy, nitro, protected hydroxy, NH_2, NHR^b, or NR^bR^c, C_1-C_6 alkyl, C_6-C_{10} aryl, C_6-C_{10} heteroaryl, C_3-C_8 heterocyclyl, a ligand, a tethered ligand, or when taken together with R^{44} or R^{46} forms $-OCH_2O-$;

R^{46} is hydrogen, halo, hydroxy, nitro, protected hydroxy, NH_2, NHR^b, or NR^bR^c, C_1-C_6 alkyl, C_6-C_{10} aryl, C_6-C_{10} heteroaryl, C_3-C_8 heterocyclyl, a ligand, a tethered ligand, or when taken together with R^{45} or R^{47} forms $-OCH_2O-$;

R^{47} is hydrogen, halo, hydroxy, nitro, protected hydroxy, NH_2, NHR^b, or NR^bR^c, C_1-C_6 alkyl, C_6-C_{10} aryl, C_6-C_{10} heteroaryl, C_3-C_8 heterocyclyl, a ligand, a tethered ligand, or when taken together with R^{46} or R^{48} forms $-OCH_2O-$;

R^{48} is hydrogen, halo, hydroxy, nitro, protected hydroxy, NH_2, NHR^b, or NR^bR^c, C_1-C_6 alkyl, C_6-C_{10} aryl, C_6-C_{10} heteroaryl, C_3-C_8 heterocyclyl, a ligand, a tethered ligand, or when taken together with R^{47} forms $-OCH_2O-$;

R^{49} R^{50}, R^{51}, R^{52}, R^{53}, R^{54}, R^{57}, R^{58}, R^{59}, R^{60}, R^{61}, R^{62}, R^{63}, R^{64}, R^{65}, R^{66}, R^{67}, R^{68}, R^{69}, R^{70}, R^{71}, and R^{72} are each independently selected from hydrogen, halo, hydroxy, nitro, protected hydroxy, NH_2, NHR^b, or NR^bR^c, C_1-C_6 alkyl, C_2-C_6 alkynyl, C_6-C_{10} aryl, C_6-C_{10} heteroaryl, C_3-C_8 heterocyclyl, $NC(O)R^{17}$, or $NC(O)R^o$;

R^{55} is hydrogen, halo, hydroxy, nitro, protected hydroxy, NH_2, NHR^b, or NR^bR^c, C_1-C_6 alkyl, C_2-C_6 alkynyl, C_6-C_{10} aryl, C_6-C_{10} heteroaryl, C_3-C_8 heterocyclyl, $NC(O)R^{17}$, or $NC(O)R^o$, or when taken together with R^{56} forms a fused aromatic ring which may be optionally substituted;

R^{56} is hydrogen, halo, hydroxy, nitro, protected hydroxy, NH_2, NHR^b, or NR^bR^c, C_1-C_6 alkyl, C_2-C_6 alkynyl, C_6-C_{10} aryl, C_6-C_{10} heteroaryl, C_3-C_8 heterocyclyl, $NC(O)R^{17}$, or $NC(O)R^o$, or when taken together with R^{55} forms a fused aromatic ring which may be optionally substituted;

X is O, S, or Se;

Y is O or S;

L is $-C(O)(CH_2)_qC(O)-$, or $-C(O)(CH_2)_qS-$;

Provided that R^1, R^2, and R^3 cannot all be hydrogen; further provided that when R^5 is hydrogen, R^6 cannot be NH_2, NH(protecting group), or NH(iBu); further provided that when R^{12} is hydrogen and R^8 and R^{11} together form a double bond between the carbon and nitrogen atoms to which they are attached, R^9 and R^{10} cannot both be hydrogen; further provided that when X and Y are O, R^{19} is hydrogen, and R^{21} and R^{23} together form a double bond between the carbon atoms to which they are attached, R^{20} cannot be hydrogen or CH_3;

R^a is glycinyl, threonyl, or norvalyl, each of which may optionally be partially or fully protected;

R^b is C_1-C_6 alkyl or a nitrogen protecting group;

R^c is C_1-C_6 alkyl;

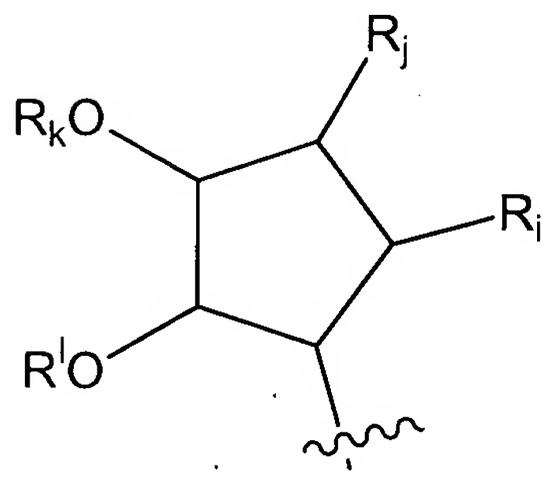
R^d is hydrogen, hydroxy, protected hydroxy, or OOH;

R^e is hydrogen, a nitrogen protecting group, or $COOR^g$;

R^f is hydrogen, or C_1-C_6 alkyl;

R^g is C_1-C_{10} alkyl;

R^h is hydrogen, or



R_i and R_j when taken together forms a double bond between the carbon atoms to which they are attached, or R_i and R_j when taken together form -O- between the carbon atoms to which they are attached;

R_k and R^l are each, independently, hydrogen, a hydroxyl protecting group,a sugar, or a fully or partially protected sugar;

R^m is C_1-C_4 alkyl optionally substituted with COOH;

R^o is alkyl optionally substituted with halo, hydroxy, nitro, protected hydroxy, NH_2, NHR^b, or NR^bR^c, C_1-C_6 alkyl, C_2-C_6 alkynyl, C_6-C_{10} aryl, C_6-C_{10} heteroaryl, C_3-C_8 heterocyclyl, $NC(O)R^{17}$, or $NC(O)R^o$;

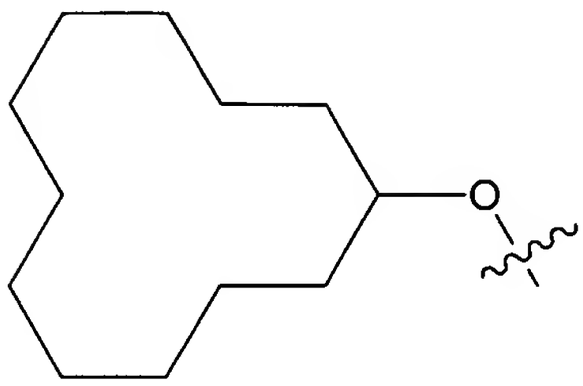
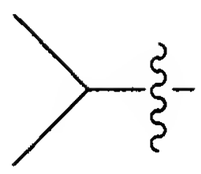
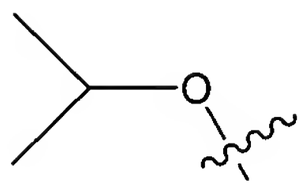
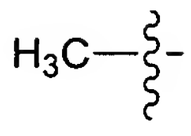
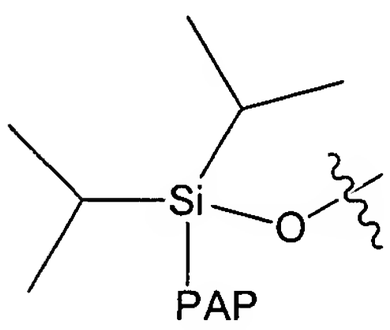
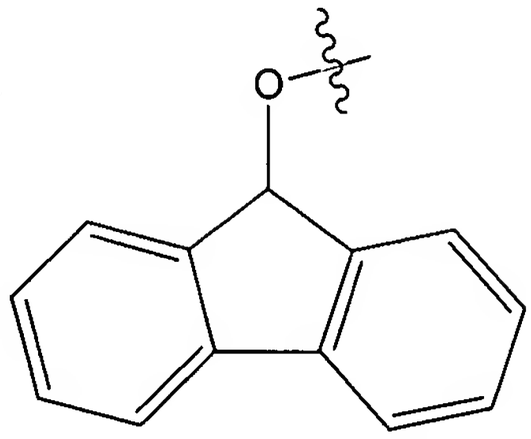
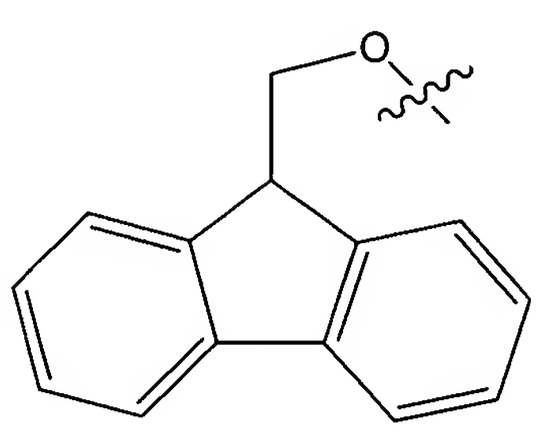
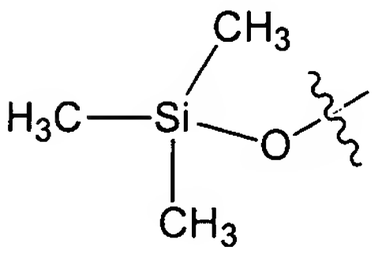
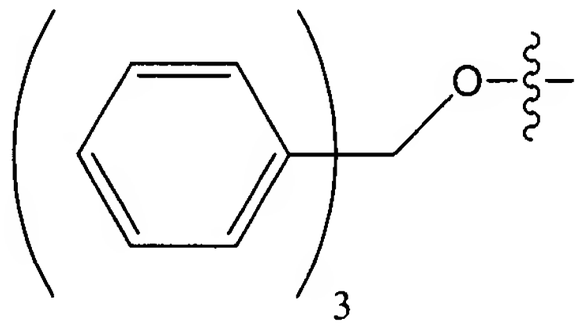
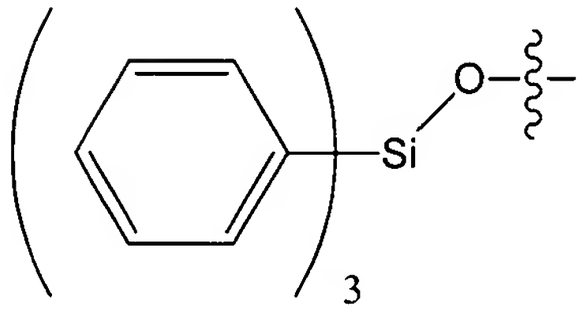
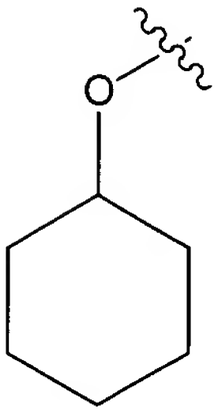
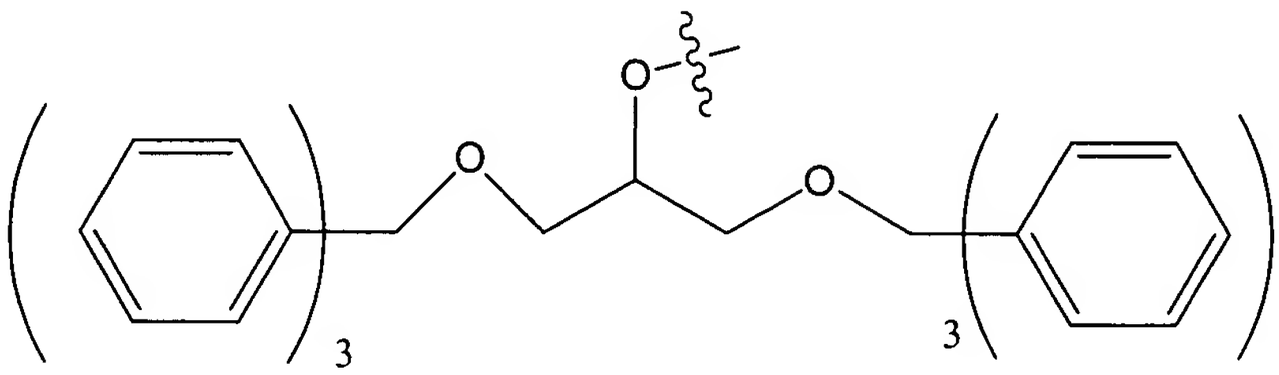
n is 1-4; and

q is 0-4.

2-17. (Canceled)

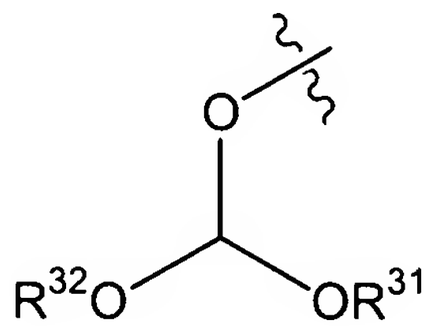
18. (Original) The monomer of claim1, wherein R^{28} is isopropyl.

19. (Original) The monomer of claim 1, wherein $X^{5'}$, $X^{5''}$, and $X^{5'''}$ are any combination of the following formula:

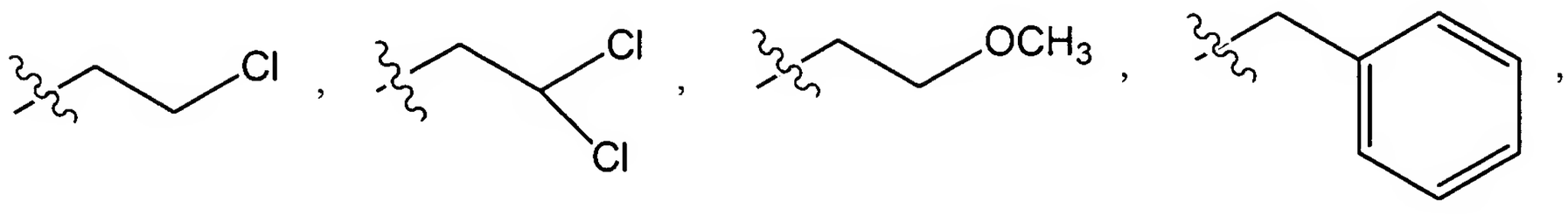
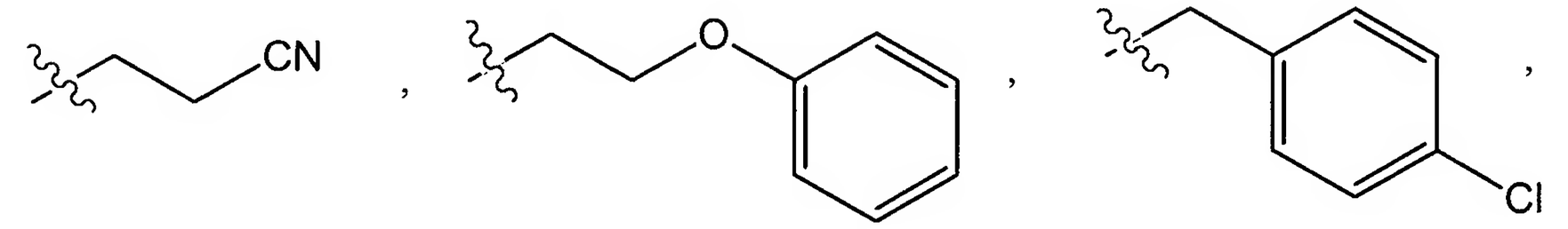
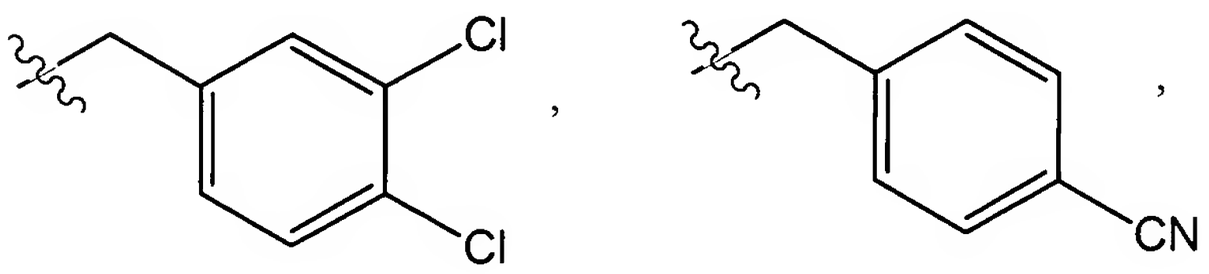
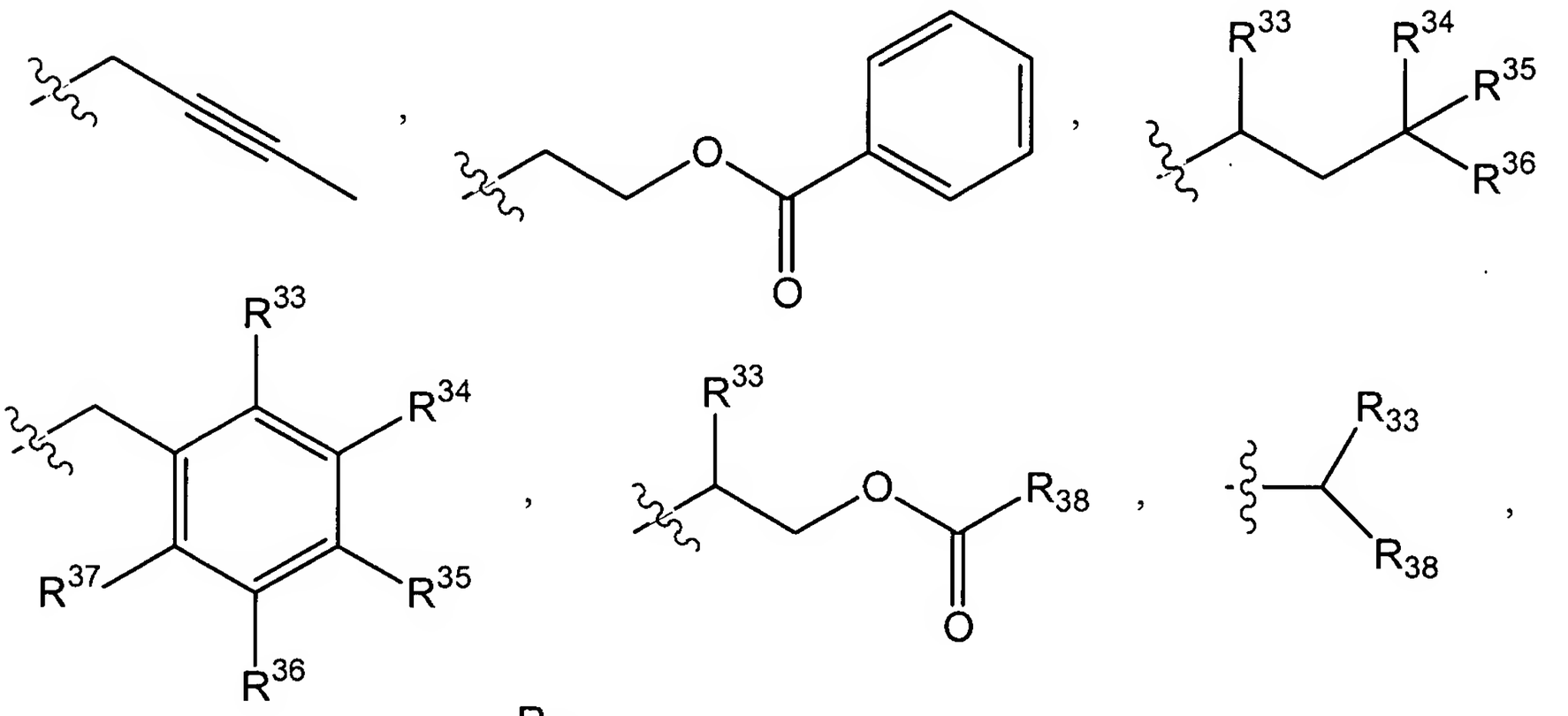
20. (Original) The compound of claim 1, wherein $X^{5'}$ and $X^{5''}$ are siloxy and $X^{5'''}$ is cycloalkoxy.

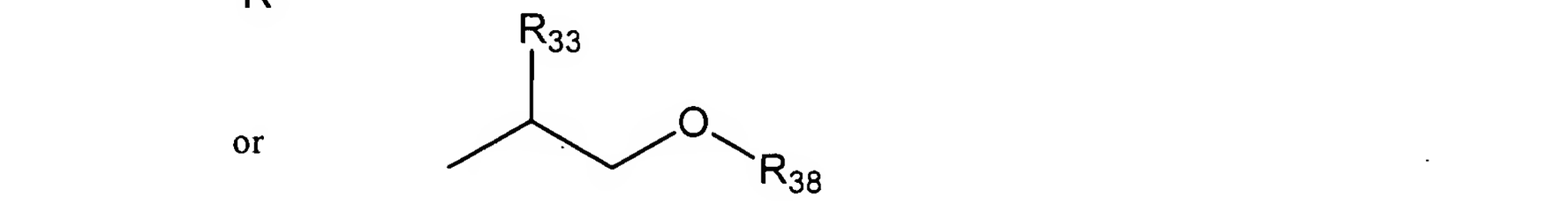
21. (Original) The monomer of claim 1, wherein the orthoester protecting group has a formula (III):



(III)

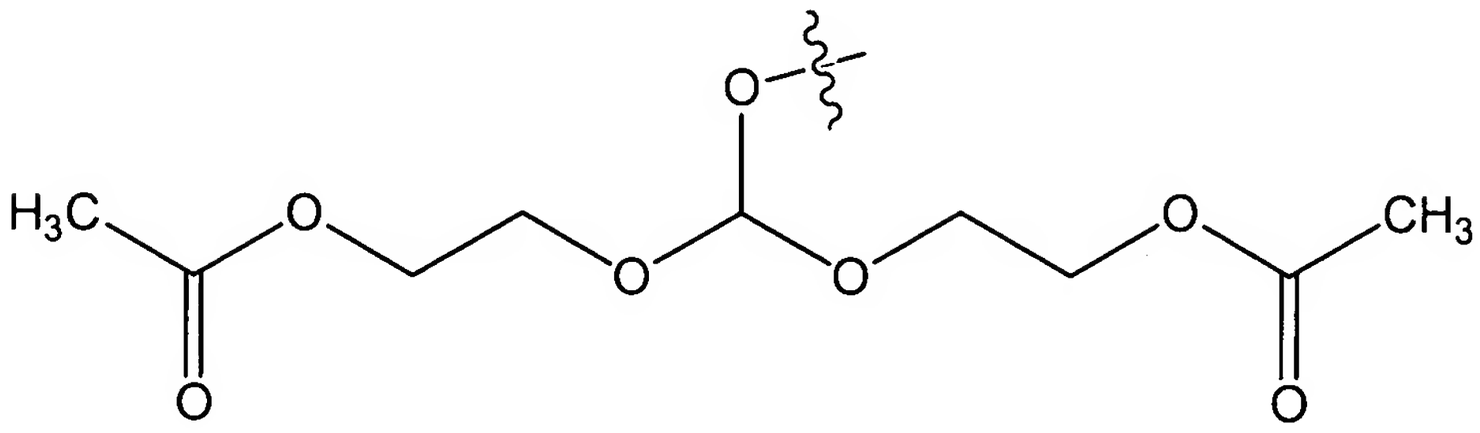
22. (Original) The monomer of claim 21, wherein R^{31} and R^{32} are the same or different and are any combination of the following formulae:



wherein R^{33}, R^{34}, R^{35}, R^{36}, and R^{37} is a compatible ligand, or hydrogen, or halogen, alkyl, or cyano substituent, and R^{38} is compatible ligand.

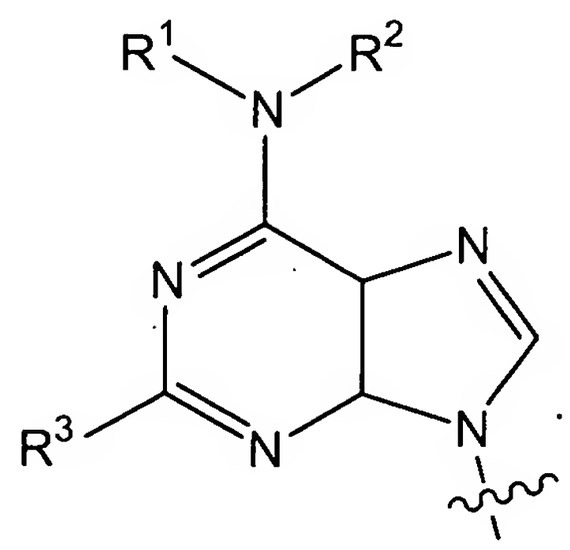
23. (Original) The monomer of claim 21, wherein the orthoester is:



24. (Original) The monomer of claim 1, wherein R^{29} is a fluoride-stable polystyrene based solid support or PEG.

25-40. (Canceled)

41. (Original) The monomer of claim 1, wherein B is selected from the group consisting of:



2-aminoadeninyl

2-methyladeninyl,

N6-methyladeninyl,

2-methylthio-N6-methyladeninyl,

N6-isopentenyladeninyl,

2-methylthio-N6-isopentenyladeninyl,

N6-(cis-hydroxyisopentenyl)adeninyl,

2-methylthio-N6-(cis-hydroxyisopentenyl) adeninyl,

N6-glycinylcarbamoyladeninyl,

N6-threonylcarbamoyladeninyl,

2-methylthio-N6-threonyl carbamoyladeninyl,

N6-methyl-N6-threonylcarbamoyladeninyl,

N6-hydroxynorvalylcarbamoyladeninyl,

2-methylthio-N6-hydroxynorvalyl carbamoyladeninyl,

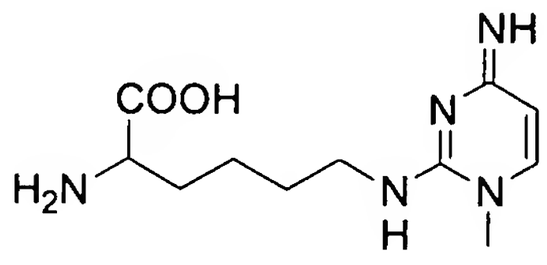
N6,N6-dimethyladeninyl,

3-methylcytosinyl,

5-methylcytosinyl,

2-thiocytosinyl,

5-formylcytosinyl,



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N4-methylcytosinyl,

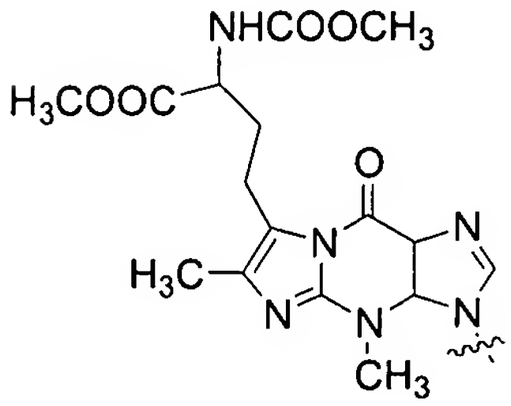
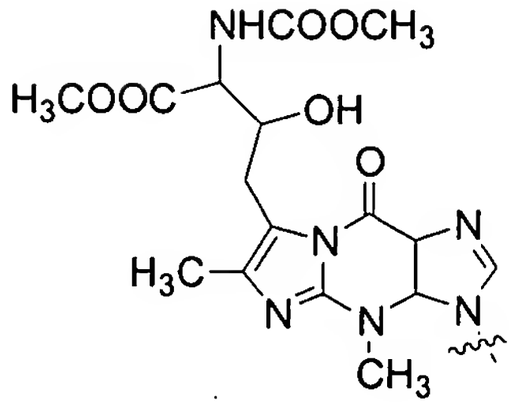
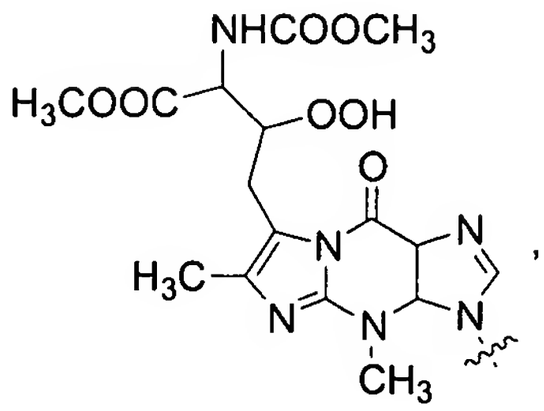
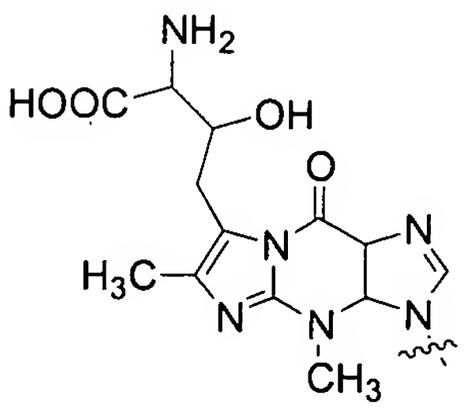
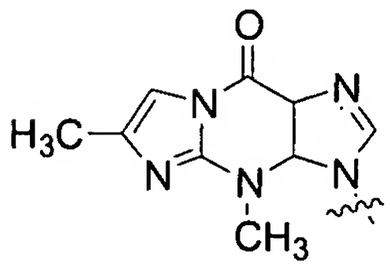
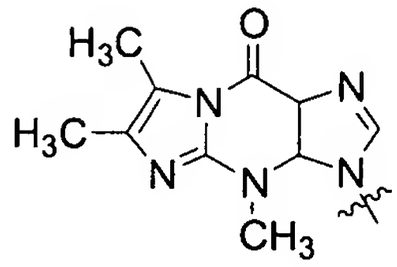
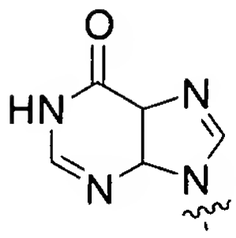
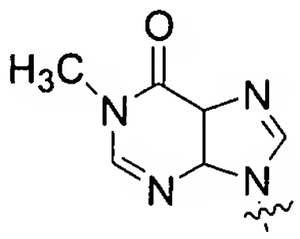
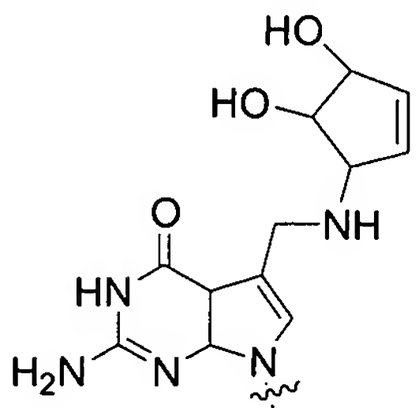
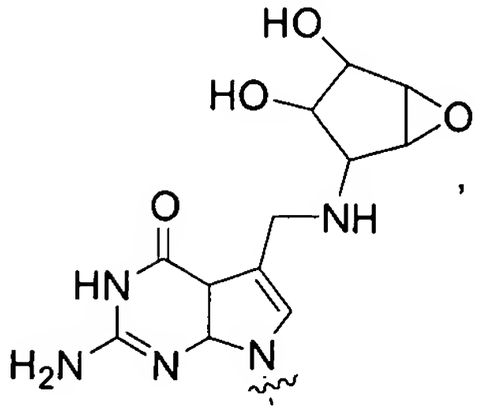
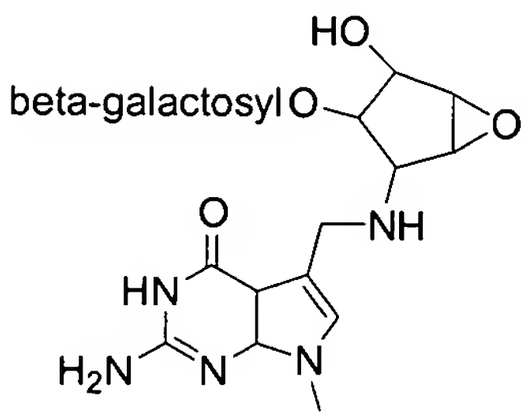
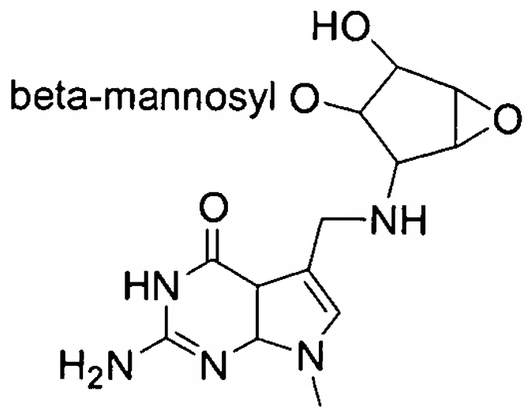
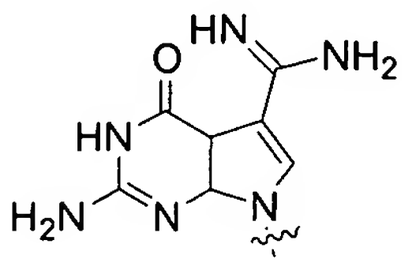
5-hydroxymethylcytosinyl,

1-methylguaninyl,

N2-methylguaninyl,

7-methylguaninyl,

N2,N2-dimethylguaninyl,

N2,7-dimethylguaninyl,

N2,N2,7-trimethylguaninyl,

1-methylguaninyl,

7-cyano-7-deazaguaninyl,

7-aminomethyl-7-deazaguaninyl,

pseudouracilyl,

dihydrouracilyl,

5-methyluracilyl,

1-methylpseudouracilyl,

2-thiouracilyl,

4-thiouracilyl,

5-methyl-2-thiouracilyl,

3-(3-amino-3-carboxypropyl)uracilyl,

5-hydroxyuracilyl,

5-methoxyuracilyl,

uracilyl 5-oxyacetic acid,

uracilyl 5-oxyacetic acid methyl ester,

5-(carboxyhydroxymethyl)uracilyl,

5-(carboxyhydroxymethyl)uracilyl methyl ester,

5-methoxycarbonylmethyluracilyl,

5-methoxycarbonylmethyl-2-thiouracilyl,

5-aminomethyl-2-thiouracilyl,

5-methylaminomethyluracilyl,

5-methylaminomethyl-2-thiouracilyl,

5-methylaminomethyl-2-selenouracilyl,

5-carbamoylmethyluracilyl,

5-carboxymethylaminomethyluracilyl,

5-carboxymethylaminomethyl-2-thiouracilyl,

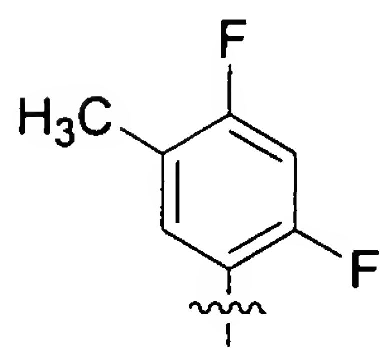
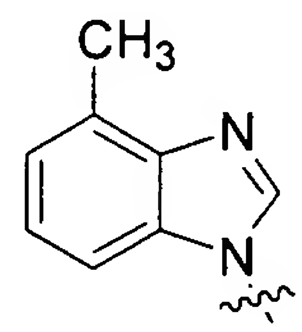
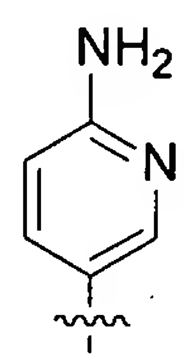
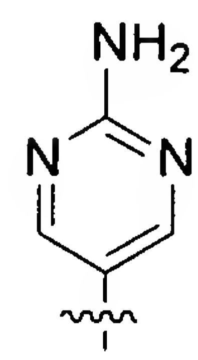
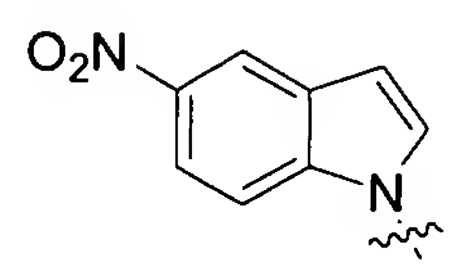
3-methyluracilyl,

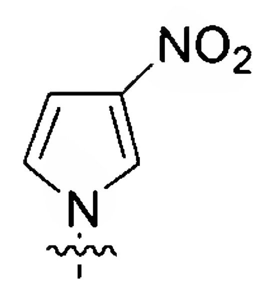
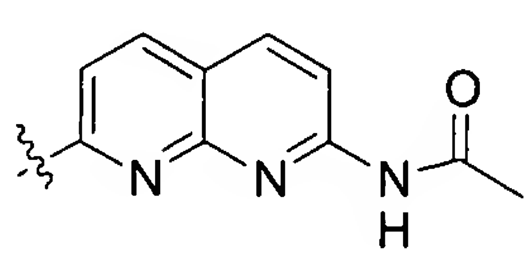
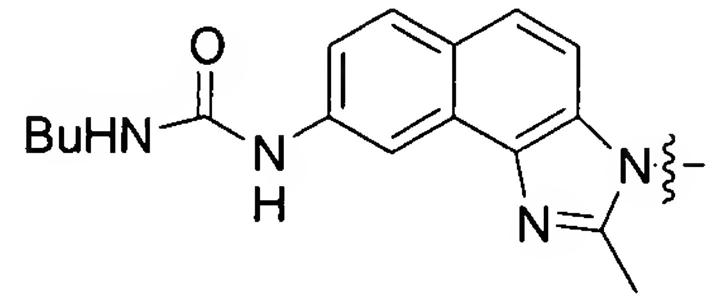
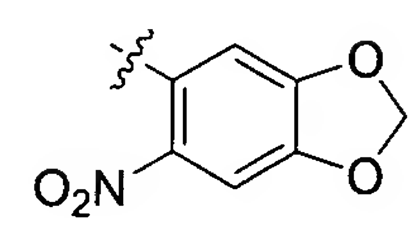
1-methyl-3-(3-amino-3-carboxypropyl) pseudouracilyl,

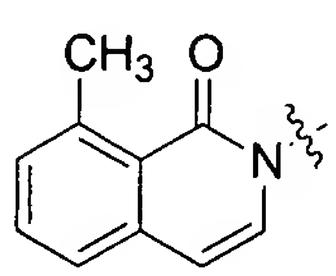
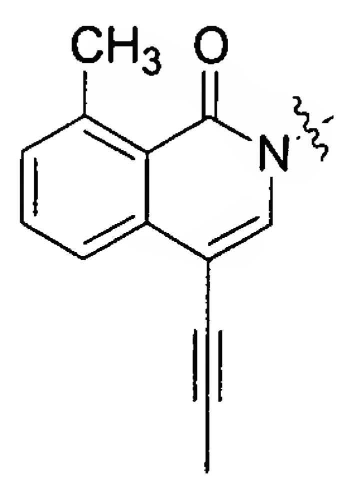
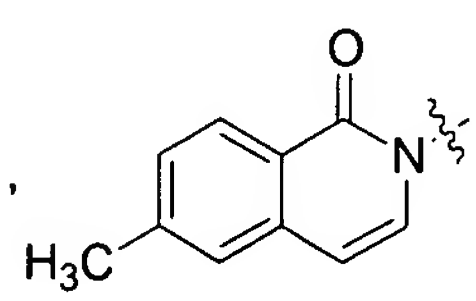
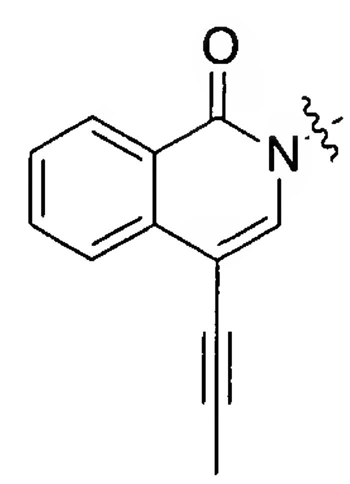
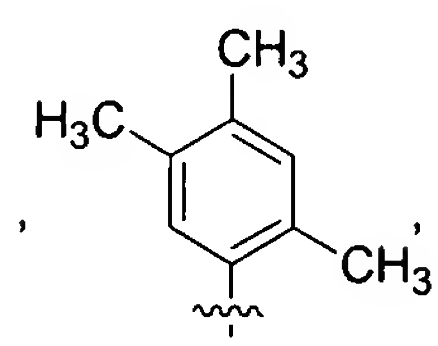
5-carboxymethyluracilyl,

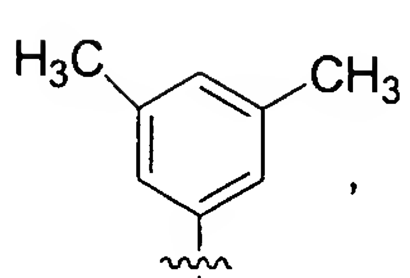
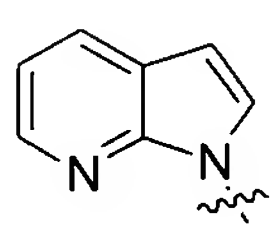
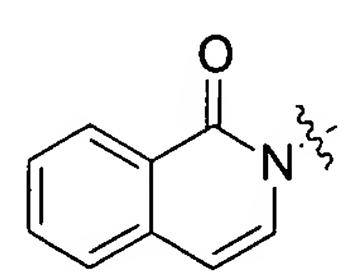
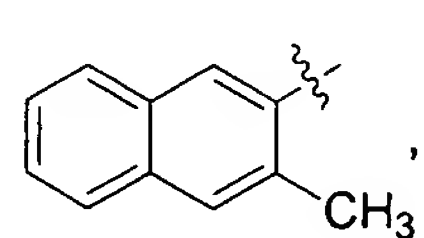
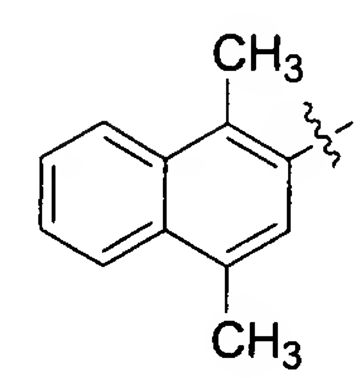
5-methyldihydrouracilyl,

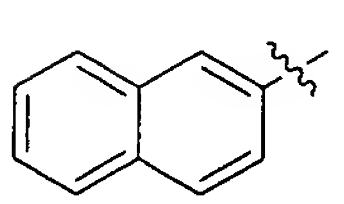
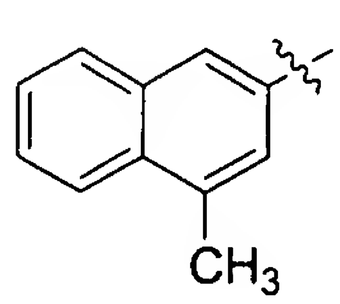
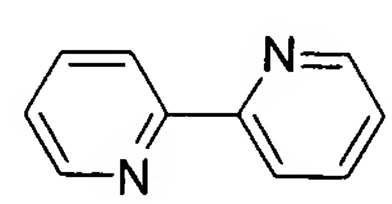
3-methylpseudouracilyl,

 ,  ,  ,  ,  ,

 ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  , and  .

42. (Original) The monomer of claim 1, wherein X^2 is $-OC[OCH_2CH_2OC(O)CH_3]_2$; R^{27} is CH_3; R^{28} is $(CH_3)_2CH$-; X5' and X5" are trimethylsiloxy; X5"' is cyclododecyloxy; and B is selected from the group consisting of:

2-aminoadeninyl,

2-methyladeninyl,

N6-methyladeninyl,

2-methylthio-N6-methyladeninyl,

N6-isopentenyladeninyl,

2-methylthio-N6-isopentenyladeninyl,

N6-(cis-hydroxyisopentenyl)adeninyl,

2-methylthio-N6-(cis-hydroxyisopentenyl) adeninyl,

N6-glycinylcarbamoyladeninyl,

N6-threonylcarbamoyladeninyl,

2-methylthio-N6-threonyl carbamoyladeninyl,

N6-methyl-N6-threonylcarbamoyladeninyl,

N6-hydroxynorvalylcarbamoyladeninyl,

2-methylthio-N6-hydroxynorvalyl carbamoyladeninyl,

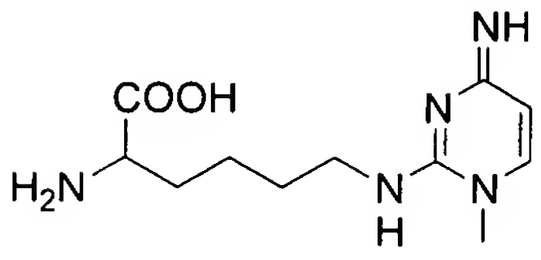
N6,N6-dimethyladeninyl,

3-methylcytosinyl,

5-methylcytosinyl,

2-thiocytosinyl,

5-formylcytosinyl,



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N4-methylcytosinyl,

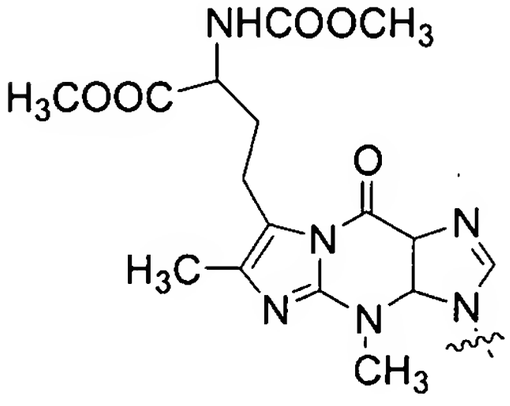
5-hydroxymethylcytosinyl,

1-methylguaninyl,

N2-methylguaninyl,

7-methylguaninyl,

N2,N2-dimethylguaninyl,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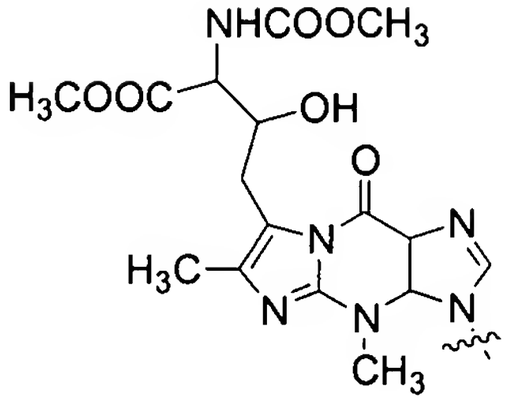
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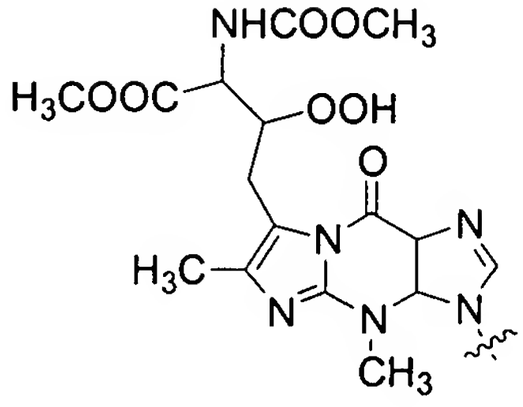
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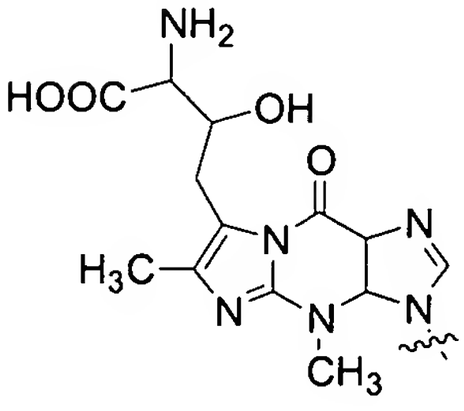
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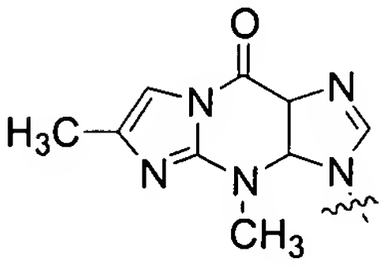
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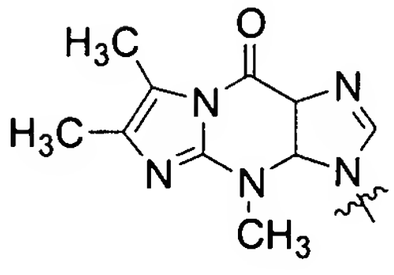
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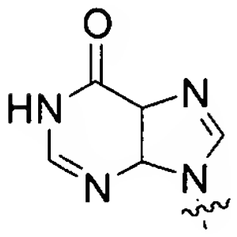
N2,7-dimethylguaninyl,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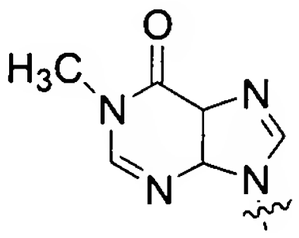
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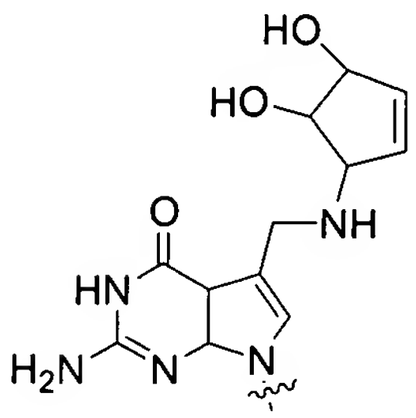
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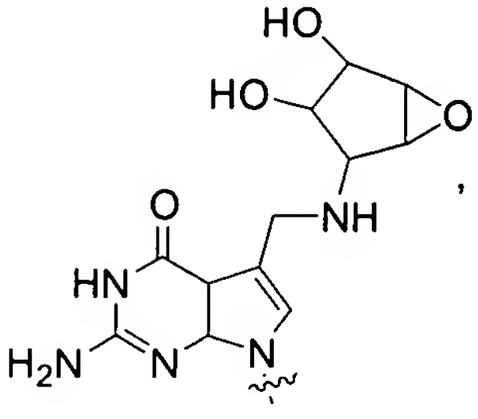
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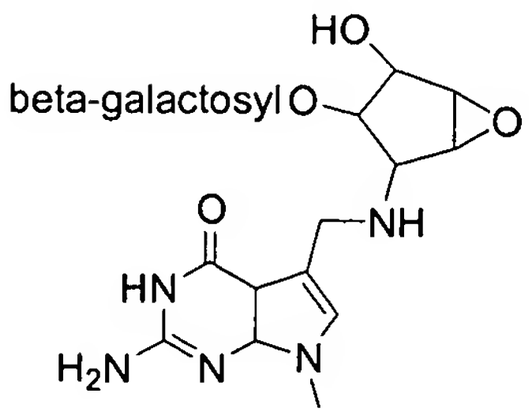
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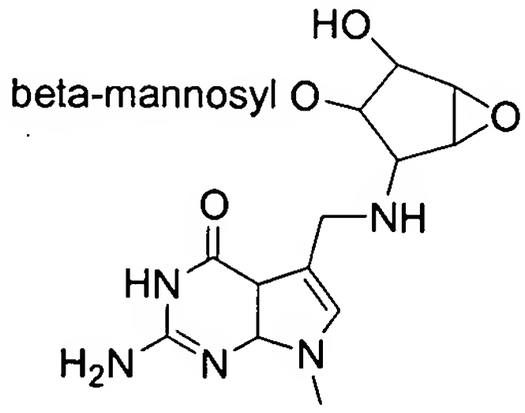
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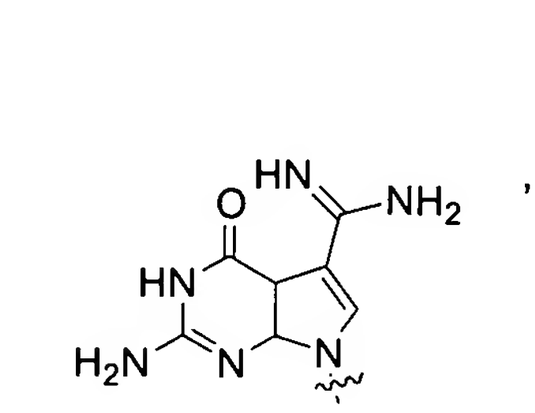
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N2,N2,7-trimethylguaninyl,

1-methylguaninyl,

7-cyano-7-deazaguaninyl,

7-aminomethyl-7-deazaguaninyl,

pseudouracilyl,

dihydrouracilyl,

5-methyluracilyl,

1-methylpseudouracilyl,

2-thiouracilyl,

4-thiouracilyl

5-methyl-2-thiouracilyl,

3-(3-amino-3-carboxypropyl)uracilyl,

5-hydroxyuracilyl,

5-methoxyuracilyl,

uracilyl 5-oxyacetic acid,

uracilyl 5-oxyacetic acid methyl ester,

5-(carboxyhydroxymethyl)uracilyl,

5-(carboxyhydroxymethyl)uracilyl methyl ester,

5-methoxycarbonylmethyluracilyl,

5-methoxycarbonylmethyl-2-thiouracilyl,

5-aminomethyl-2-thiouracilyl,

5-methylaminomethyluracilyl,

5-methylaminomethyl-2-thiouracilyl,

5-methylaminomethyl-2-selenouracilyl,

5-carbamoylmethyluracilyl,

5-carboxymethylaminomethyluracilyl,

5-carboxymethylaminomethyl-2-thiouracilyl,

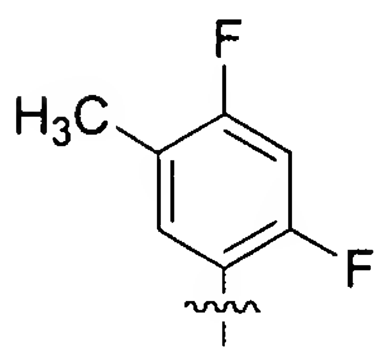
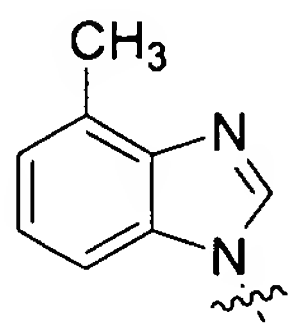
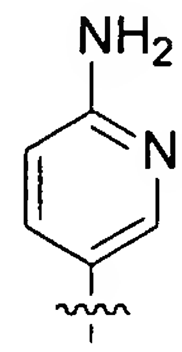
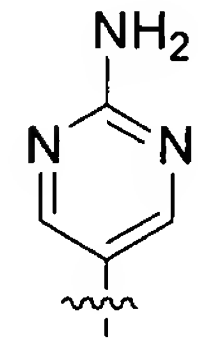
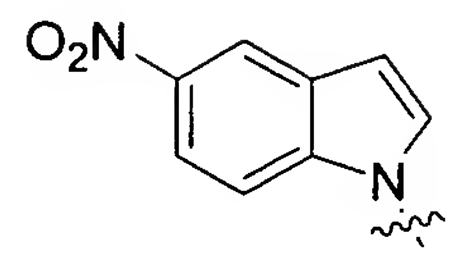
3-methyluracilyl,

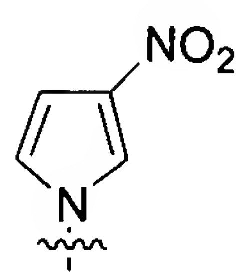
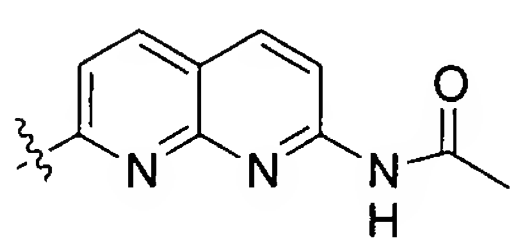
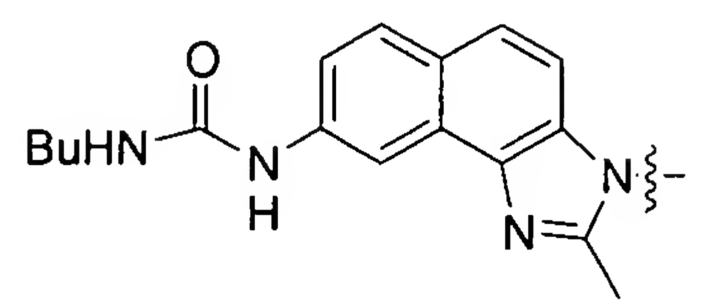
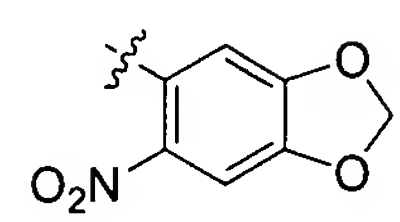
1-methyl-3-(3-amino-3-carboxypropyl) pseudouracilyl,

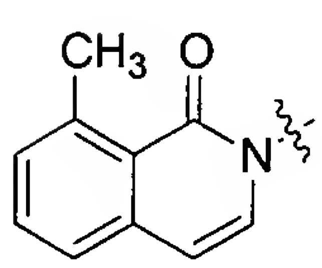
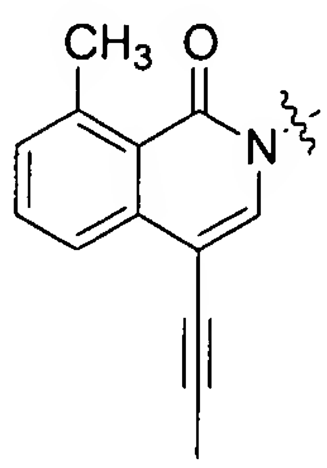
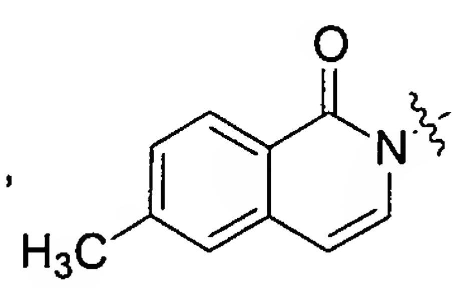
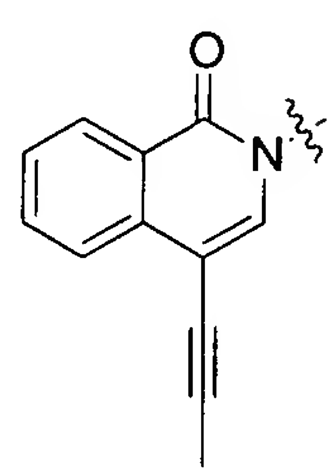
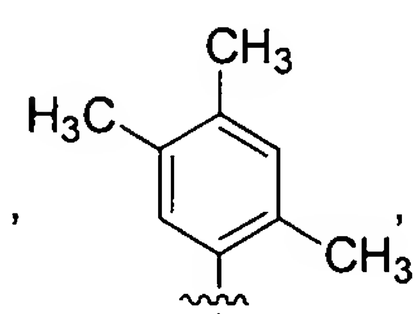
5-carboxymethyluracilyl,

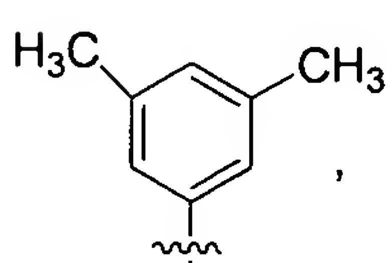
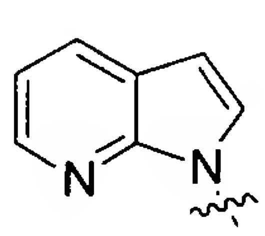
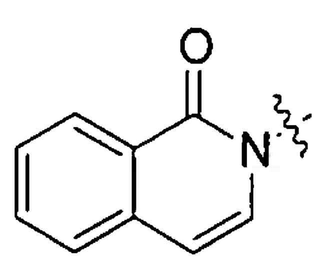
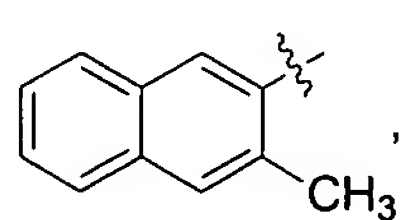
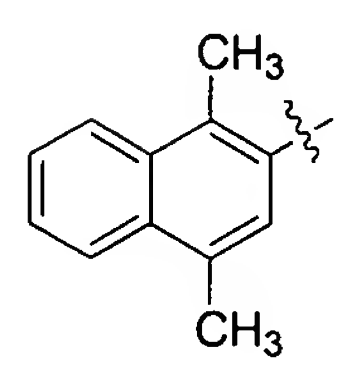
5-methyldihydrouracilyl,

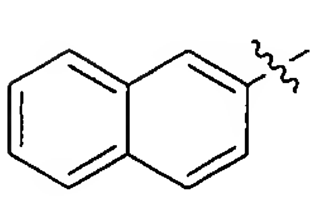
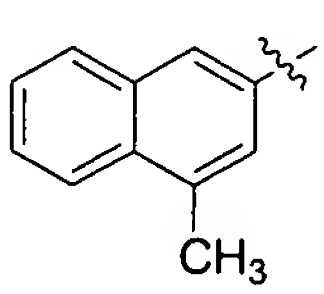
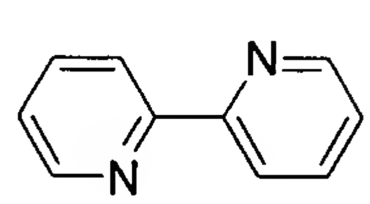
3-methylpseudouracilyl,

 ,  ,  ,  ,  ,

 ,  ,  ,  ,

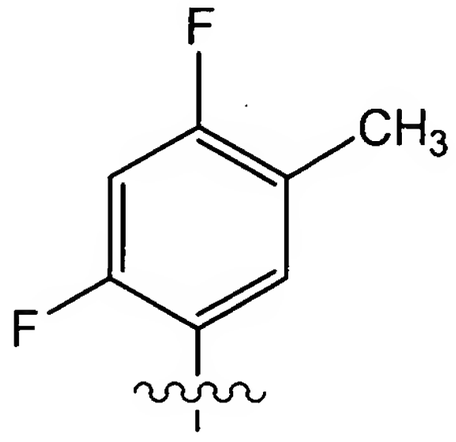
 ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  , and  .

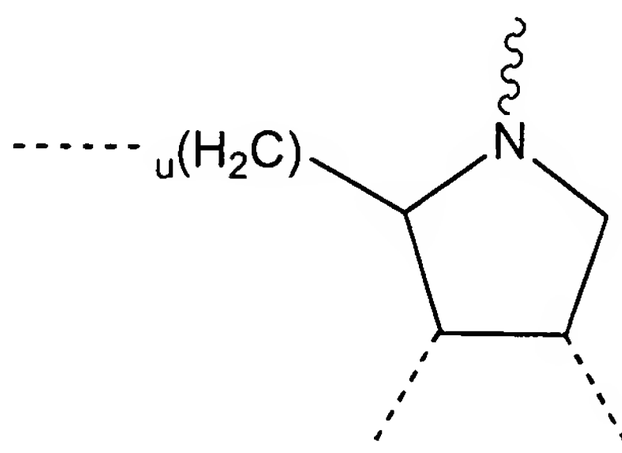
43. (Original) The monomer of claim 1, wherein X^2 is fluoro.

44. (Original) The monomer of claim 1, wherein B is:



45. (Original) The monomer of claim 1, wherein B is substituted or unsubstituted aryl attached to a tethered or untethered ligand.

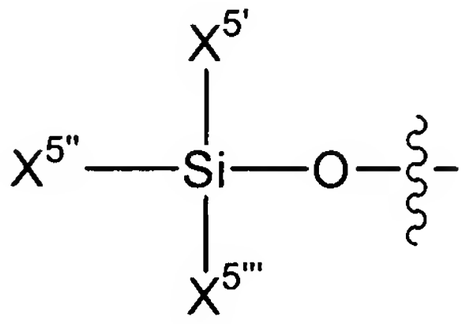
46. (Original) A protected monomer having a formula:



in which

u is 1 or 2; the wavy line represents a point of attachment for a ligand or a tethered ligand; and the dotted lines represent points of attachment for a first functionalized hydroxyl group; a second functionalized hydroxyl group; and an unfunctionalized hydroxyl group, a protected hydroxyl group, or hydrogen.

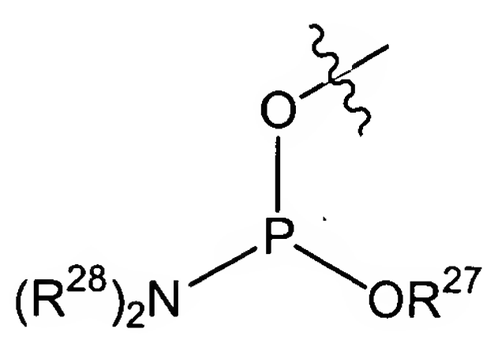
47. (Original) The monomer of claim 46, wherein the first functionalized hydroxyl group has the formula:



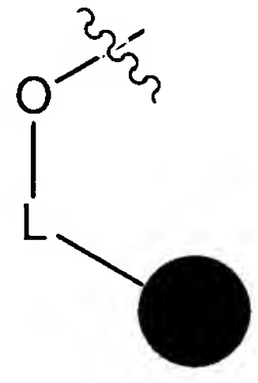
; in which

$X^{5'}$, $X^{5''}$, and $X^{5'''}$ include at least one alkoxy or siloxy substituent.

48. (Original) The monomer of claim 46, wherein the second functionalized hydroxyl group has one of the following formulas:



or



; in which

R^{27} is C_1-C_6 alkyl optionally substituted with cyano or C_2-C_6 alkenyl; R^{28} is C_1-C_{10} alkyl; ● is a solid or liquid support reagent; and L is a linker.

49. (Original) The monomer of claim 46, wherein the ligand is a targeting group.

50. (Original) The monomer of claim 49, wherein the targeting group is a lipid, steroid, vitamin, carbohydrate, polyamine, amino acid, peptide, peptide mimetic or cleaving molecule.

51. (Original) The monomer of claim 50, wherein the steroid is cholesterol.

52. (Original) The monomer of claim 46, wherein the ligand is a diagnostic group.

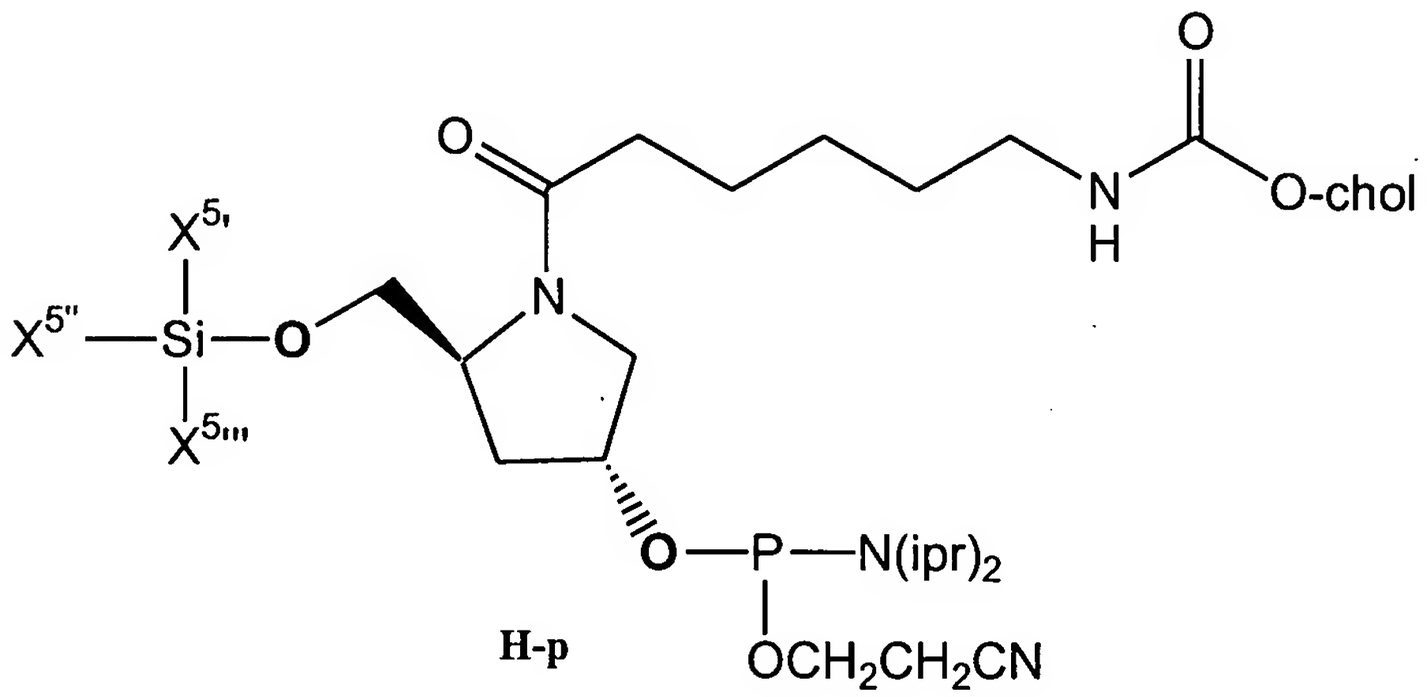
53. (Original) The monomer of claim 52, wherein the diagnostic group is biotin, a fluorophore, an antibody or an antigen.

54. (Original) The monomer of claim 46, wherein the ligand has a formula $(G)C(=H)NHR^n$, in which G is -O-, -NH-, or $-CH_2-$; H is O or NH; and R^n is H, C_1-C_6 alkyl, C_6-C_{10} aryl, or C_5-C_{10} heteroaryl.

55. (Original) The monomer of claim 46, wherein the monomer has a tethered ligand.

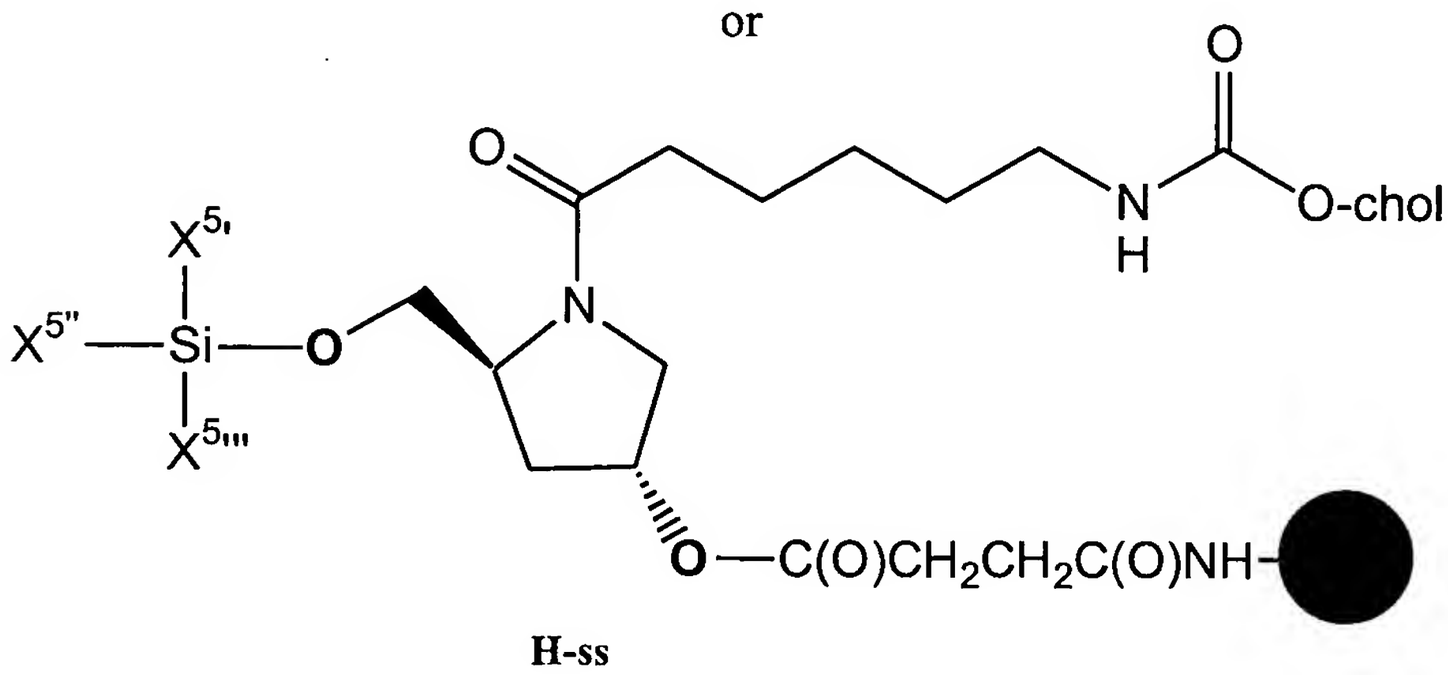
56. (Original) The monomer of claim 55, wherein the ligand is tethered with a tether selected from the group consisting of: $-C(O)-(CH_2)_s-C(O)-$(ligand); $-C(O)-(CH_2)_s-C(O)O-$(ligand); $-C(O)-O-$(ligand); $-C(O)-(CH_2)_s-NH-$; $-C(O)-(CH_2)_s-NH-C(O)-$(ligand); $-C(O)-(CH_2)_s-$(ligand); $-C(O)-NH-$(ligand); $-C(O)-$(ligand); $-(CH_2)_s-C(O)-$(ligand); $-(CH_2)_s-C(O)O-$(ligand); $-(CH_2)_s-$(ligand); $-(CH_2)_s-NH-$; and $-(CH_2)_s-NH-C(O)-$(ligand), wherein s is 0-6.

57. (Original) The monomer of claim 46, wherein the monomer has the formula:



H-p

or



H-ss

wherein, $X^{5'}$, $X^{5''}$, and $X^{5'''}$ include at least one alkoxy or siloxy substituent, ipr is an isopropyl group, and chol is a cholesterol radical.

58. (Currently amended) An iRNA agent having a monomer of claim 1 ~~or 46~~.

59. (Currently amended) A method of making an iRNA agent, the method comprising providing ~~an iRNA agent~~ a first RNA sequence having a monomer of claim 1 ~~or 46~~ and allowing ~~it~~ the first RNA sequence to anneal to a complementary RNA sequence to form an iRNA agent.

60. (New) A method of synthesizing an iRNA agent, the method comprising incorporating a monomer of claim 1 into a first RNA sequence and allowing the first RNA sequence to anneal to a complementary RNA sequence to form an iRNA agent.